

Amendments to the Claims:¹

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Withdrawn) A biologically active TGF- β family member fusion protein competent to refold under suitable refolding conditions, comprising:

a TGF- β family protein C-terminal seven cysteine domain, comprising a finger 1 subdomain, a finger 2 subdomain, and a heel subdomain; and

a heterologous leader sequence domain operatively linked to said C-terminal domain.
2. (Withdrawn) The fusion protein of claim 1 wherein said leader sequence is selected from the group consisting of a tissue-targeting domain, a molecular-targeting domain, a metal-binding domain, a protein-binding domain, a ceramic-binding domain, a hydroxyapatite-binding domain, and a collagen-binding domain.
3. (Withdrawn) The fusion protein of claim 2 wherein said tissue-targeting domain binds to a bone matrix protein.
4. (Withdrawn) The fusion protein of claim 2 wherein said tissue-targeting domain binds to a cell surface molecule.

¹ The Amendments to the Claims are the same as those submitted in applicants' November 9, 2009 Amendment and Reply After Final.

5. (Withdrawn) The fusion protein of claim 4 wherein said cell surface molecule is on an osteoprogenitor cell or a chondrocyte.

6. (Currently amended) A latent OP-1 fusion protein, comprising:

an OP-1 C-terminal seven cysteine domain, comprising a finger 1 subdomain comprising amino acid residues 2-29 of SEQ ID NO:55, a finger 2 subdomain comprising amino acid residues 68-98 of SEQ ID NO:55, and a heel subdomain comprising amino acid residues 35-65 of SEQ ID NO:55; and

a cleavable leader sequence operably linked to said OP-1 C-terminal domain wherein said cleavable leader sequence is selected from the group consisting of a leader sequence derived from a TGF- β family protein other than OP-1, a metal-binding domain, a protein-binding domain, a ceramic-binding domain, a hydroxyapatite-binding domain and a collagen-binding domain; wherein said cleavable leader sequence inhibits the biological activity associated with said OP-1 C-terminal domain; wherein said OP-1 C-terminal domain becomes active upon cleavage of a part or all of said leader sequence; and wherein said latent protein is a refolded protein.

7. (Previously presented) The latent OP-1 fusion protein of claim 6 wherein a part of the leader sequence is cleaved.

8. (Currently amended) The latent OP-1 fusion protein of claim 6 wherein said cleavable leader sequence is separated from said C-terminal domain by at least seven residues.

9. (Currently amended) The latent OP-1 fusion protein of claim 6 wherein said cleavable leader sequence is a leader sequence derived from a TGF- β family protein other than OP-1.

10. (Withdrawn) A biologically active TGF- β family member protein mutant competent to refold under suitable refolding conditions, comprising:

a TGF- β family member protein C-terminal seven cysteine domain, comprising a finger 1 subdomain, a finger 2 subdomain, and a heel subdomain; and

a leader sequence domain operatively linked to said C-terminal domain, whereby a part or all of said leader sequence is truncated.

11. (Withdrawn) The protein mutant of claim 10 wherein said truncation is carried out by protease cleavage.

12. (Withdrawn) The protein mutant of claim 11 wherein said protease is trypsin.

13. (Withdrawn) The protein mutant of claim 10 wherein said truncation is carried out by chemical cleavage.

14. (Withdrawn) The protein mutant of claim 13 wherein said chemical cleavage is acid cleavage.

15. (Withdrawn) The protein mutant of claim 10 wherein at least one basic residue of said leader sequence is removed.

16. (Withdrawn) The protein mutant of claim 10 wherein said protein mutant consists essentially of amino acid sequence SEQ ID NO. 69.

17. (Withdrawn) A biologically active heterodimer of TGF- β family member proteins, comprising:

a first subunit being a TGF- β family member fusion protein; and

a second subunit selected from the group consisting of a TGF- β family member fusion protein different from that of the first subunit and a wild type TGF- β family protein.

18. (Withdrawn) The heterodimer of claim 16, wherein said wild type TGF- β family protein is selected from the group consisting of TGF- β 1, TGF- β -2, TGF- β 3, TGF- β 4, TGF- β 5, dpp, Vg-1, Vgr-1, 60A, BMP-2A, BMP-3, BMP-4, BMP-5, BMP-6, Dorsalin, OP-1, OP-2, OP-3, GDF-1, GDF-3, GDF-9, Inhibin α , Inhibin β A and Inhibin β B.

19. (Withdrawn) A method of purifying a heterodimer of TGF- β family proteins, said method comprising:

- (a) providing a first TGF- β family protein subunit;
- (b) providing a second TGF- β family protein subunit different from said first subunit;
- (c) mixing said first subunit and said second subunit under suitable refolding conditions to generate a mixture comprising
 - (i) a first homodimer comprising two of said first TGF- β family protein subunits;
 - (ii) a second homodimer comprising two of said second TGF- β family protein subunits; and
 - (iii) a heterodimer comprising one of said first TGF- β family subunits and one of said second TGF- β family subunits;

wherein said heterodimer is separable from said first homodimer and said second homodimer; and

- (d) separating said heterodimer from said first homodimer and said second homodimer.

20.-21. (Canceled).